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IN THE UNITED STATES PATENTAND TRADEMARK OFFICE

Application No.:	tba	Art Unit:	1614
Filed:	tba	Examiner:	R. Cook
1st Inventor:	ODAKA, H. et al.	Allowed:	
For:	Pharmaceutical Composition	Batch:	
Atty. Dkt. No.	2530 US1P	Paper No.:	

PRELIMINARY AMENDMENT

BOX NEW APPLICATION
Assistant Commissioner for Patents
Washington, D.C. 20231
Sir:

Applicants respectfully request that the following preliminary amendments be made, prior to calculating the filing fee.

AMENDMENT

In the Specification

Please insert before "Technical Field" as the first sentence the following statement:

- - This Application is a continuation of US Patent Application Serial Number 09/380,059, filed 8/25/99 and now US Patent _____, which was the National Stage of International Application Serial No. PCT/JP99/03496, filed June 29, 1999. - -

Please amend page 2, lines 26-27 by deleting

[patients accompanied by a high-degree of obesity]

and inserting therefor - - obese patients - -

Please amend page 21, line 3 by deleting [central] and substituting therefor - - controller - -

In the Claims

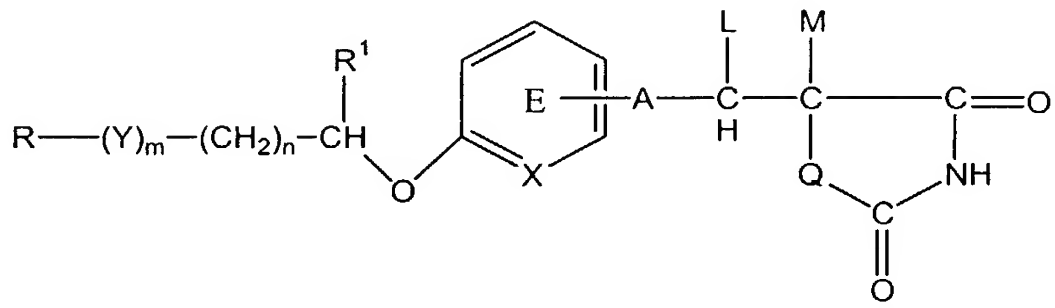
Please Cancel Claims 8-10 inclusive and Cancel Claims 12-21 inclusive, without prejudice to the filing of future continuing applications.

Please add the following NEW Claims 22-27.

Please rewrite the following claims 1-7 and 11 to read as follows:

1. (Amended) A method for lowering the concentration of glycosylated hemoglobin in a mammal in need thereof, which comprises administering to said mammal an effective amount of an insulin sensitizer in combination with an anorectic.

2. (Amended) The method according to claim 1, wherein the insulin sensitizer is a compound of the formula:



wherein R represents a hydrocarbon group or a heterocyclic group, each of which may be substituted; Y represents a group of the formula: -CO-, -CH(OH)- or -NR^3- where R^3 represents an alkyl group that may be substituted; m is 0 or 1; n is 0, 1 or 2; X represents CH or N; A represents a chemical bond or a bivalent aliphatic hydrocarbon group having 1 to 7 carbon atoms; Q represents oxygen or sulfur; R^1 represents hydrogen or an alkyl group; ring E may have further 1 to 4 substituents, which may form a ring in combination with R^1; L and M respectively represent hydrogen or may be combined with each other to form a chemical bond; or a salt thereof.

3. (Amended) The method according to claim 1, wherein the insulin sensitizer is pioglitazone, troglitazone, rosiglitazone, 4-[4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxy]benzyl]isoxazolidin-3,5-dione, 5-[[6-(2-fluorobenzyloxy)-2-naphthyl]methyl]-2,4-thiazolidinedione or their salts.

4. (Amended) The method according to claim 2, wherein the compound of the formula (I) or salt thereof is pioglitazone hydrochloride.

5. (Amended) The method according to claim 1, wherein the anorectic is a β-adrenaline receptor agonist.

A2

6. (Amended) The method according to claim 5, wherein the β-adrenaline receptor agonist is mazindol.

7. (Amended) The method according to claim 1, wherein the insulin sensitizer is pioglitazone hydrochloride and the anorectic is mazindol.

A3

11. (Amended) The method according to claim 2 , wherein the compound of the formula (I) or salt thereof is rosiglitazone or its maleate.

A4

22. (new) The method according to claim 1, wherein the anorectic is selected from the group consisting of α-adrenaline receptor antagonists, β-adrenaline receptor agonists, dopamine receptor agonists, serotonin receptor agonists, 5-HT agonists, cimetidine and ergoset.

23. (new) The method according to claim 1, wherein the anorectic is selected from the group consisting of leptin and its analogues; leptin receptor agonists; leptin resistance-improving agents; neuropeptide Y antagonists; cholecystokinin agonists; glucagon-like peptide 1 or its analogues or its agonists; galannin antagonist; glucagon agonists; melanin-concentrating hormone agonists; melanocortin agonists; enterostatin agonists; tripeptidylpeptidase II inhibitors; and corticotropin releasing hormone or its analogues or its agonists.

24. (new) The method according to claim 1, wherein the anorectic is sibutramine.

25. (new) The method according to claim 1, wherein the insulin sensitizer is pioglitazone or its salt, and the anorectic is sibutramine.

A4

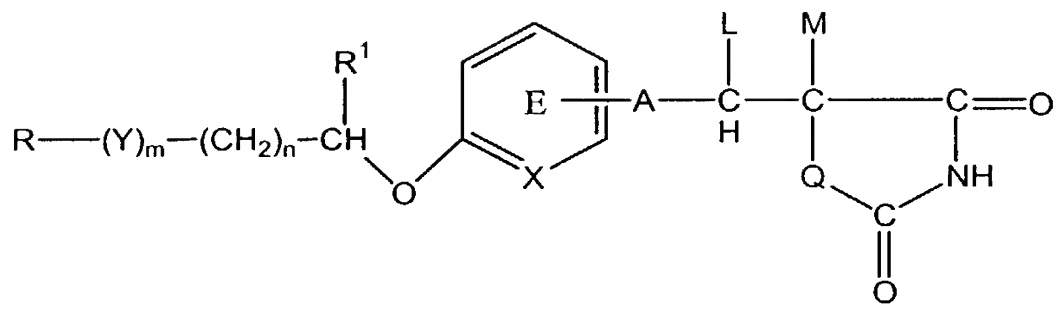
26. (new) The method according to claim 1, wherein the insulin sensitizer and the anorectic are administered to the mammal concomitantly.

27. (new) The method according to claim 1, wherein the insulin sensitizer and the anorectic are administered to the mammal separately.

MARK-UP OF THE CLAIMS

1. (Amended) [A pharmaceutical composition which comprises an insulin sensitizer in combination with an anorectic] A method for lowering the concentration of glycosylated hemoglobin in a mammal in need thereof, which comprises administering to said mammal an effective amount of an insulin sensitizer in combination with an anorectic.

2. (Amended) [A pharmaceutical composition] The method according to claim 1, wherein the insulin sensitizer is a compound of the formula:



wherein R represents a hydrocarbon group or a heterocyclic group, each of which may be substituted; Y represents a group of the formula: -CO-, -CH(OH)- or $-NR^3-$ where R^3 represents an alkyl group that may be substituted; m is 0 or 1; n is 0, 1 or 2; X represents CH or N; A represents a chemical bond or a bivalent aliphatic hydrocarbon group having 1 to 7 carbon atoms; Q represents oxygen or sulfur; R^1 represents hydrogen or an alkyl group; ring E may have further 1 to 4 substituents, which may form a ring in combination with R^1; L and M respectively represent hydrogen or may be combined with each other to form a chemical bond; or a salt thereof.

3. (Amended) [A pharmaceutical composition] The method according to claim 1, wherein the insulin sensitizer is pioglitazone [hydrochloride], troglitazone, rosiglitazone, [or] 4-[4-[2-(5-methyl-2-phenyloxazol-4-yl)ethoxy]benzyl]isoxazolidin-3,5-dione, 5-[[6-(2-fluorobenzyloxy)-2-naphthyl]methyl]-2,4-thiazolidinedione or their salts.

4. (Amended) [A pharmaceutical composition] The method according to claim 2, wherein the compound of the formula (I) or salt thereof is pioglitazone hydrochloride.

5. (Amended) [A pharmaceutical composition] The method according to claim 1, wherein the anorectic is a [central anorectic] β-adrenaline receptor agonist.

6. (Amended) [A pharmaceutical composition] The method according to claim 5, wherein the [central anorectic] β-adrenaline receptor agonist is mazindol.

7. (Amended) [A pharmaceutical composition] The method according to claim 1, wherein the insulin sensitizer is pioglitazone hydrochloride and the anorectic is mazindol.

Cancel Claims 8-10 inclusive

11. (Amended) [A pharmaceutical composition] The method according to claim 2 , wherein the compound of the formula (I) or salt thereof is rosiglitazone or its maleate.

Cancel Claims 12-21 inclusive.

22. (new) The method according to claim 1, wherein the anorectic is selected from the group consisting of α-adrenaline receptor antagonists, β-adrenaline receptor agonists, dopamine receptor agonists, serotonin receptor agonists, 5-HT agonists, cimetidine and ergoset.

23. (new) The method according to claim 1, wherein the anorectic is selected from the group consisting of leptin and its analogues; leptin receptor agonists; leptin resistance-improving agents; neuropeptide Y antagonists; cholecystokinin agonists; glucagon-like peptide 1 or its analogues or its agonists; galannin antagonist; glucagon agonists; melanin-concentrating hormone agonists; melanocortin agonists; enterostatin agonists; tripeptidylpeptidase II inhibitors; and corticotropin releasing hormone or its analogues or its agonists.

24. (new) The method according to claim 1, wherein the anorectic is sibutramine.

25. (new) The method according to claim 1, wherein the insulin sensitizer is pioglitazone or its salt, and the anorectic is sibutramine.

26. (new) The method according to claim 1, wherein the insulin sensitizer and the anorectic are administered to the mammal concomitantly.

27. (new) The method according to claim 1, wherein the insulin sensitizer and the anorectic are administered to the mammal separately.

REMARKS

I. Amendments

In the Specification

A statement describing related patent applications has been added to the specification.

Clarification of the translation of certain phrases in the specification, objected to by the Examiner in the parent case has been made.

In the Claims

After entry of the Preliminary Amendment, Claims 1-7, 11, and 22-27 (14 claims total) are pending in this case. The only independent claim is Claim 1.

II. Conclusion

Consideration of the claims as amended above is solicited. Early allowance of the claims is requested. Should the Examiner believe that a conference with applicants' attorney would advance prosecution of this application, she is respectfully requested to call applicants' attorney at (847) 383-3372.

Respectfully submitted,

Dated: October 29, 2001

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